IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

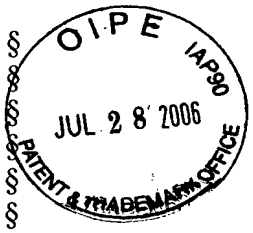
Oron YACOBY-ZEEVI

Serial No.: 09/260,037

Filed: March 2, 1999

For: Introducing A Biological Material Into A Patient

Examiner: Richard G. Hutson



Group Art Unit: 1652

Attorney Docket: 00/20442

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 U.S.C. SECTION 1.131

Sir:

I, Iris Pecker, declare as follows:

1) I am the Iris Pecker who is an inventor in applications related to the subject application, including U.S. Pat. No. 5,968,822 (the '822 patent).

2) Cells require heparan sulfate on their surface in order for heparanase to externally adhere to them. However, not all cells have heparan sulfate. CHO 745 cells, deficient in heparan sulfate for example, have not shown external adherence for this reason. In the case of High Five cells or Sf21 cells taught in the '822 patent, I am not aware of any evidence of their having heparan sulfate on their surface or of secreted heparanase externally adhering to these cells.

3) Furthermore, cells that have been genetically modified to express heparanase and cells that have had heparanase added to them can be distinguished by ones skilled in the art.

4) For example, when the pro-enzyme form of heparanase (P60) is added to cells, it can be detected in the cells by Western blot. However, P60 is not detected in cells that naturally express heparanase, as well as in most cells that express heparanase through genetic modification, including the High Five and Sf21 cells taught in the '822 patent.

5) Moreover, genetically modifying mammalian cells so that they can secrete heparanase was not obvious at the time of the subject invention. Firstly, in most genetically modified mammalian cells which express heparanase, recombinant heparanase can not be detected in the culture medium, but rather inside the cells. While the '822 patent teaches heparanase secretion in insect cells, secretion of heparanase from mammalian cells was obtained only when the signal peptide of heparanase was replaced by a secretion signal peptide.

6) Secondly, since most of the cell lines commonly used for expression of recombinant proteins have a basal heparanase expression it would have been hard to distinguish the two forms of expression by the ECM assay used by those skilled in the art at the time.

I declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willfully false statements are punishable by fine or imprisonment under 18 U.S.C. Section 1001 and that any such statement may jeopardize the validity of the subject application or any patent issued thereon.

Is Pecker

Dr. Iris Pecker

26/7/06

Date